REMARKS

I. Claim Status

Claims 1-2, 7-22, 27-71, 74-76, 79-105, 110-114, and 120-124 were cancelled by prior amendment. Claim 115 has been amended to correct a typographical error. Claim 144 is cancelled by the present amendment. Accordingly, claims 3-6, 23-26, 72-73, 77-78, 106-109, 115-119, and 125-143 are pending. All of the pending claims read on the elected species.

II. Information Disclosure Statement

Pursuant to the Examiner's request, a corrected version of the Information Disclosure Statement, previously submitted on December 4, 2000 to the Office, was filed on October 16, 2007.

III. Priority/Specification

A. Benefit Claim

The Examiner alleges that Applicants have not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. § 119(e) and/or 120 . Specifically, the Examiner alleges that the priority documents fail to provide support pursuant to 35 U.S.C. § 112, first paragraph for the pending claims. Applicants respectfully disagree. Relevant support can be found in the priority documents, *inter alia*, at the citations provided in the table below. A cursory review of the priority documents was done and the Table below is not meant to be complete. Applicants believe that the citations listed below are sufficient to establish priority relevant to the art rejections raised.

Claim	USSN 60/119,766	USSN 60/148,848
3	p. 3, lines 1-3 ("The invention provides a method for high throughput spectrometry, that is used, for example, to monitor enzyme reactions, e.g., at the rate of about 100 samples per hour or more."); p. 4, lines 8-10 ("Because these steps are in parallel, at least 100 cell colonies are screened for presence or activity of the one or more non-column-separated component in less than an hour.");	

	p. 5, lines 21-26 ("The automatic sampler is a sample handler that transports samples from the off-line parallel purification system to the mass handler that transports samples from the off-line parallel purification system to the mass spectrometer for injection and analysis. It can transport, e.g., at least 100 samples in about an hour."); p. 32, lines 3-5 ("Flow injection analysis of off-line purified samples using tandem mass spectroscopy allowed sample analysis of 100 samples in less than one hour."	
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24	p. 23, lines 25-26 ("Tandem mass spectrometry uses the fragmentation of precursor ions to fragment ions within a triple quadrupole MS."); p. 24, lines 3-5 ("Triple quadropole mass spectrometers allow MS/MS analysis of samples. For example, a triple quadropole mass spectrometer with electrospray and atmospheric pressure chemical ionization sources, such as a Finnigan TSQ 7000, is optionally used."); p. 27, lines 19-23 ("A solution of 1 mM atrazine in acetonitrile was prepared and used to develop a MS/MS method on the triple quadruple mass spectrometer (Finnigan TSQ 7000)."); p. 31, lines 24-28 ("<u>D: Flow-injection analysis on electrospray tandem mass spectrometer</u> Triple quadrupole mass spectrometers allow MS/MS analysis of samples.")	
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72	p. 22, lines 12-13 ("In one aspect, cells are centrifuged and the buffer added to the supernatant. Substrate is added and cell debris filtered off in a parallel fashion.").	
73	p. 27, lines 14-17 ("The entire reaction mixture was transferred onto a filter plate	

	and any solid cell debris and precipitates removed by filtration. The samples were injected directly into the electrospray mass spectrometer by flow injection and analyzed by tandem mass spectroscopy."); p. 31, lines 11-12 ("Substrate was added and cell debris filtered off in a parallel fashion"); p. 31, lines 16-17 ("Since the cells (*E. coli*) were partially lysed, cell debris, DNA and protein impurities were precipitated with ethanol and removed by filtration.".	
77	p. 5, lines 21-23 ("The automatic sampler is a sample handler that transports samples from the off-line parallel purification system to the mass spectrometer for injection and analysis. It can transport, e.g., at least 100 samples in about an hour.")	
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106	p. 3, lines 14-16 ("The invention provides a method for high throughput mass spectrometry, that is used, for example, to monitor enzyme reactions, e.g., at the rate of about 100 samples per hour or more."); p. 4, lines 8-10 ("Because these steps are in parallel, at least 100 cell colonies are screened for presence or activity of the one or more non-column-separated component in less than an hour.")	
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117	p. 23, lines 25-26 ("Tandem mass spectrometry uses the fragmentation of precursor ions to fragment ions within a triple quadrupole MS."); p. 24, lines 3-5 ("Triple quadropole mass spectrometers allow MS/MS analysis of samples. For	

	example, a triple quadropole mass spectrometer with electrospray and atmospheric pressure chemical ionization sources, such as a Finnigan TSQ 7000, is optionally used."); p. 27, lines 19-23 ("A solution of 1 mM atrazine in acetonitrile was prepared and used to develop a MS/MS method on the triple quadruple mass spectrometer (Finnigan TSQ 7000)."); p. 31, lines 24-28 ("D: Flow-injection analysis on electrospray tandem mass spectrometer Triple quadrupole mass spectrometers allow MS/MS analysis of samples.")	
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125	p. 5, lines 21-23 ("The automatic sampler is a sample handler that transports samples from the off-line parallel purification system to the mass spectrometer for injection and analysis. It can transport, e.g., at least 100 samples in about an hour.")	
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127	Claim 1 (A method of performing high throughput mass spectrometry screening, the method comprising: (i) growing a cell colony; (ii) purifying one or more non-column-separated component from the cell colony, the purifying comprising an off-line parallel adjustment of cell colony growing conditions; and, (iii) performing flow-injection analysis using electrospray tandem mass spectrometry, thereby obtaining mass-to-charge ratio data and providing high throughput mass spectrometry screening of the one or more non-column-separated component."); Figure 4; p. 12, lines 7-12 ("To analyze enzyme reactions using high-throughput mass spectrometry, first a single colony of cells must be picked and grown. Second, enzyme products are generated using whole cells, complete or partial cell lysates, or purified enzymes to which	

	substrates have been added. Third, the products generated from the biological matrix are purified in an off-line parallel purification system. Fourth, flow injection analysis is performed using tandem mass spectrometry."); p. 17, lines 28-30 ("In one embodiment of the present invention a cell is provided that has been transformed with a plasmid containing one or more members of a library of related gene sequences."); p. 18, lines 29-30 ("Cells are then transfected or transformed with one or more of the above library members using standard technology well known to those of skill in the art."); p. 19, lines 4 ("In general, any type of cells can be used as a recipient of evolved genes."), 20-29 ("In the present invention, single colonies of cells are picked directly from transformation plates into 1536, 384 or 96 microtiter wells or cell growth plates with appropriate growth media, such as LB, using the Q-bot from Genetrix. The maximum speed of the Q-bot is 4000 colonies per hour. The microtiter plates are incubated in a special plate shaker for cell growth. Each single colony is grown up to uniformity (this is optionally achieved by automating the process and providing temperature and humidity controlled incubators. Automating inoculum size and culture conditions provides the desired) in a single microtitre well on the cell growth plate. In one aspect, library members, e.g., cells, viral plaques, spores or the like, are separated on solid media to produce individual colonies or plaques.") ; p. 29, line 29 to p. 30, line 2 ("Using an automated colony picker (e.g., the Q-bot, Genetix, U.K.), colonies are identified, picked and 10,000 different mutants inoculated into 96 or 384 well microtiter dishes, that optionally contain two 3 mm glass balls/well."; p. 10, lines 10-14 ("As used herein, 'biological matrix' refers to the fluid, substance, or reaction mixture or	

	growth medium in which a cell is grown. The products and reactants of interest in the invention are optionally generated and/or purified in the biological matrix. The biological matrix is typically similar to the native environmental conditions of the enzyme or substance of interest."); p. 12, line 30 to p. 13, line 2 ("Making libraries includes the construction of recombinant nucleic acids and the expression of genes in transfected host cells."); p. 14, lines 1-3 ("Methods of transducing cells, including plant and animal cells, with nucleic acids as in library construction are generally available, as are methods of expressing proteins encoded by such nucleic acids."); p. 22, lines 12-13 ("In one aspect, cells are centrifuged and the buffer added to the supernatant. Substrate is added and cell debris filtered off in a parallel fashion."); p. 22, lines 19-21 ("E. coli. Cells are partially lysed, and all cell debris, DNA and protein impurities are precipitated with ethanol and removed by filtration."); p. 27, lines 14-17 ("The entire reaction mixture was transferred onto a filter plate and any solid cell debris and precipitates removed by filtration. The samples were injected directly into the eletrospray mass spectrometer by flow injection and analyzed by tandem mass spectroscopy."); p. 27, lines 27-28 ("Bacterial cell growth, reaction and sample workup were performed in parallel fashion as described above."); p. 31, lines 11-12 ("Substrate was added and cell debris filtered off in a parallel fashion."); p. 31, lines 17-18 ("Since the cells (*E. coli*) were partially lysed, cell debris, DNA and protein impurities were precipitated with ethanol and removed by filtration."); p. 11, lines 21-22 ("Using the method of the present invention, a sample is injected directly into a MS without any column separation and analyzed instantly."); p. 4, lines 11-16 ("The one or	

	more non-column-separated component is a protein, a protein binding molecule, a carbohydrate, a carbohydrate binding molecule, an enzyme, an enzyme substrate, a product of an enzyme catalyzed reaction, a nucleic acid, a product of a nucleic acid catalyzed reaction, a substrate with one or more hydrophobic moieties, an inorganic ion, an oligosaccharide, a hydrophobic molecule, a briatine derivative, atrazine, a polyketide, or other molecule of interest."); p. 3, lines 19-21 ("The off-line parallel purification eliminates the need for liquid chromatography or a separate purification step before injection of the sample into a mass spectrometer."); p. 6, lines 13-15 ("The term 'non-column-separated component' refers to components or materials of interest that are injected into a mass spectrometer without prior separation on a chromatography column.") ; p. 27, lines 16-17 ("The samples were injected directly into the elctrospray mass spectrometer by flow injection and analyzed by tandem mass spectroscopy.")	
128	p. 20, line 18 ("Cells that contain active enzymes can be lysed . . . ."); p. 21, lines 8-10 ("The present invention provides high-throughput methods for enzyme assays with whole cells or partially or completely lysed cells."); p. 30, line 3 ("Cells that contain active enzymes are lysed . . . .")	
129	p. 30, lines 3-4 ("Cells that contain active enzymes are lysed or treated with permeabilizing agents to enable for bulky and/or strongly ionic substrates to penetrate cell walls.")	
130	p. 22, lines 9-13 ("For example, small molecule substrates of interest with hydrophobic moieties like atrazine can penetrate into E. coli. Cytoplasma without lysis of the cells. Using a volatile buffer like ammonium acetate will allow a very simple	

	cleanup. Substrate is added and cell debris filtered off in a parallel fashion"); p. 31, lines 9-10 ("As noted above in Example 1, small molecule substrates with hydrophobic moieties like atrazine penetrate into the E. coli cytoplasm without lysis.")	
131	p. 5, lines 1- 5 ("The components of the sample are optionally . . . a product of an enzyme catalyzed reaction. . . .")	
132	p. 19, lines 3-5 ("IV. Growing a cell colony In general, any type of cells can be used as a recipient of evolved genes. Cells of particular interest include many bacterial cell types. . . .")	
133	p. 19, lines 7- 8 ("Cells of interest also include eukaryotic cells. . . .")	
134	p. 4, lines 4-8 ("This production occurs in a volatile buffer, a buffer that reduces concentration of ionic species followed by a purification/clean up method such as an ion exchange resin, or the production is modified to be compatible with extraction, e.g., with an organic solvent to provide a component that can be injected directly into the mass spectrometer with no further purification.")	
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136	Claim 9 ("A method for monitoring one or more product or reactant by high throughput mass spectrometry, the method comprising: (i) providing a cell that has been transformed with a plasmid containing one or more member of a library of related gene sequences; (ii) growing a cell colony or culture from the cell; (iii) producing the one or more product or reactant from the cell colony or culture in a biological matrix, thereby producing a non-column-separated sample, (iv) purifying the non-column separated sample from the biological matrix, the purifying comprising an off-line parallel adjustment of the biological matrix used for producing the non-column separated sample; and, (v) monitoring the non-column	p. 36, line 30 to p. 37, line 11 ("To obtain the libraries of organic molecule derivatives, the substrates are contacted with the members of the library of recombinant enzymes. The enzymatic reactions can be performed in numerous ways, including the use of whole cell biotransformation, permeabilized cells, cell lysate, and purified protein, for example. Whole cell biotransformation occurs when the substrate (e.g., an organic molecule) is exposed to cells containing the library of recombinant derivatizing enzymes. The library can be expressed as a surface protein on a replicable genetic package, *e.g.*, phage or yeast display,

	separated sample by flow-injection analysis using electrosptray tandem mass spectrometery, thereby monitoring the one or more product or reactant."); claim 11 ("The method of claim 9, wherein the products or reactants are selected from: an enzyme, and a product of an enzyme catalyzed reaction."); Figure 4; p. 12, lines 7-12 ("To analyze enzyme reactions using high-throughput mass spectrometry, firsts a single colony of cells must be picked and grown. Second, enzyme products are generated using whole cells, complete or partial cell lysates, or purified enzymes to which substrates have been added. Third, the products generated from the biological matrix are purified in an off-line parallel purification system. Fourth, flow injection analysis is performed using tandem mass spectrometry."); p. 17, lines 28-30 ("In one embodiment of the present invention a cell is provided that has been transformed with a plasmid containing one or more members of a library of related gene sequences."); p. 18, lines 29-30 ("Cells are then transfected or transformed with one or more of the above library members using standard technology well known to those of skill in the art."); p. 27, lines 6-8 ("The cells were grown in a specially designed shaker for microtiter plates (Kuehner, Switzerland) at 37C overnight. The saturated cultures were diluted 20-fold into 2XYT (100uL) with Kanamycin and IPTG to initiate expression and grown again overnight at 37C."); p. 29, line 29 to p. 30, line 2 ("Each single colony was grown up in a single microtiter well to uniformity and then treated in several different ways to initiate product formation." If enzyme expression is purposely suppressed during cell growth, which is sometimes desirable, expression can be induced by removing the suppressor or adding activator molecules."); p. 10, lines	or as a secreted protein that interacts with the substrate in solution. The enzymes can also be expressed inside the cell, in which case the substrate will diffuse into the cell before the reaction occurs. In each case, the resulting product of the derivatizing enzyme activity is isolated from the cells by methods known to those of skill in the art, including, for example, centrifugation, precipitation, extraction with organic solvents, and filtration."); p. 38, lines 4-11 (The contacting of an organic molecule and other reactants with a recombinant derivatizing enzyme can be done using the entire library of enzymes at once, or with pools of recombinant enzymes from the library, or with a single recombinant enzyme in each reaction. If a pool is used, the pool can be deconvoluted to isolate the particular clone that exhibits a desired activity once an active pool had been identified using the descried methods. For example, colonies that express each member of the library of recombinant derivatizing enzymes can be placed in microtiter plates or other suitable container and subjected to high throughput screening."); p. 39, lines 13-18 ("Separation of the recombinant enzymes from other cellular components, or from reactants and the like, can be effected for example, by . . . filter with a wash solution or solvent."); p. 40, line 30 to p. 41, line 2 ("A number of analytical screening tools are available for determining the structure of compounds in a combinatorial library. For example, a number of methods are known that are capable of detecting low concentrations of compounds in a high

	10-14 ("As used herein, 'biological matrix' refers to the fluid, substance, or reaction mixture or growth medium in which a cell is grown. The products and reactants of interest in the invention are optionally generated and/or purified in the biological matrix. The biological matrix is typically similar to the native environmental conditions of the enzyme or substrate of interest."); claim 9 (iii) ("producing the one or more product or reactant from the cell colony or culture in a biological matrix, thereby producing a non-column-separated sample"); claim 23(i) ("a cell growth plate for growing cell samples and reacting one or more of an enzyme, an enzyme substrate, and a enzyme product."); p. 22, lines 12-13 ("In one aspect, cells are centrifuged and the buffer added to the supernatant. Substrate is added and cell debris filtered off in a parallel fashion."); p. 22, lines 19-21 ("Oligosaccharides are cleaned up by removing all ionic species using a mixed ion exchange resin. E. coli. Cells are partially lysed, and all cell debris, DNA and protein impurities are precipitated with ethanol and removed by filtration."); p. 27, lines 14-17 ("The entire reaction mixture was transferred onto a filter plate and any solid cell debris and precipitates removed by filtration. The samples were injected directly into the electrospray mass spectrometer by flow injection and analyzed by tandem mass spectroscopy.") p. 31, lines 11-12 ("Substrate was added and cell debris filtered off in a parallel fashion."); p. 11, lines 21-22 ("Using the method of the present invention, a sample is injected directly into a MS without any column separation and analyzed instantly."); p. 3, lines 19-21 ("The off-line parallel purification eliminates the need for liquid chromatography or a separate purification step before injection of the sample into a mass spectrometer."); p. 27,	throughput format, including flow analysis NMR and mass spectrometry.")

	lines 16-17 ("The samples were injected directly into the electrospray mass spectrometer by flow injection and analyzed by tandem mass spectroscopy.")	
137	p. 20, line 18 ("Cells that contain active enzymes can be lysed. . . ."); p. 21, lines 9-10 ("The present invention provides high-throughput methods for enzyme assays with whole cells or partially or completely lysed cells."); p. 30, line 3 ("Cells that contain active enzymes are lysed. . . .")	
138	p. 30, lines 3-4 ("Cells that contain active enzymes are lysed or treated with permeabilizing agents to enable for bulky and/or strongly ionic substrates to penetrate cell walls.")	
139	p. 19, lines 4-5 (Cells of particular interest include many bacterial cell types. . . .")	
140	p. 19, lines 7-8 ("Cells of interest also include eukaryotic cells. . . .")	
141	p. 22, lines 12-13 ("In one aspect, cells are centrifuged and the buffer added to the supernatant. Substrate is added and cell debris filtered off in a parallel fashion.").	
142	p. 27, lines 14-17 ("The entire reaction mixture was transferred onto a filter plate and any solid cell debris and precipitates removed by filtration. The samples were injected directly into the electrospray mass spectrometer by flow injection and analyzed by tandem mass spectroscopy."); p. 31, lines 11-12 ("Substrate was added and cell debris filtered off in a parallel fashion"); p. 31, lines 16-17 ("Since the cells (*E. coli*) were partially lysed, cell debris, DNA and protein impurities were precipitated with ethanol and removed by filtration.")	
143	p. 4, lines 4-8 ("This production occurs in a volatile buffer, a buffer that reduces concentration of ionic species followed by a purification/clean up method such as an ion exchange resin, or the production is modified to be compatible with extraction, e.g., with an organic solvent to provide a component	

	that can be injected directly into the mass spectrometer with no further purification.")	

Applicants wish to respectfully point out that in the April 11, 2007 Office Action, the Examiner has acknowledged that the disclosure in priority document USSN 60/119,766 is sufficient to anticipate the pending claims under 35 U.S.C. § 102(e). Given that 35 U.S.C. § 102(e) provides that "[a] person shall not be entitled to a patent unless (e) the invention was described in . . . (2) a patent granted . . . . (Section 102(e) of Title 35, emphasis added) , it is respectfully submitted that Applicants priority claim is proper.

B. Reference to benefit claim

The specification has been amended to delete reference to PCT application number PCT/US00/03686. It is consistent with continuity information provided on the ADS and filing receipt. The Specification has also been amended to provide the filing date of the '766 application. Applicants thank the examiner for pointing out this error.

IV. Objection to claim 115

Claim 115 has been amended to correct the typographical error in line 1. Withdrawal of this rejection is respectfully requested.

V. Rejections

A. 35 U.S.C. § 112, second paragraph

Claim 144 has been cancelled. Withdrawal of this rejection is respectfully requested.

B. 35 U.S.C. § 112, first paragraph

Claims 3-6, 23-26, 72, 73, 77, 78, 106-109, 115-119 and 125-144 stand rejected under 35 U.S.C. § 112, first paragraph. Specifically, the Examiner asserts that the amendments made to claims 127 and 136 constitute new matter. This rejection is respectfully traversed.

The Examiner alleges that the application does not provide support for separating cells or cell debris using "only" centrifugation and/or filtration for "any" analyte. Applicants respectfully point

out that the claims do not specify that "only" centrifugation and/or filtration are utilized. The transitional language of the claim, "comprising", does not exclude the use of the different strategies described in the specification in conjunction with the step of using centrifugation and/or filtration to remove cells and cellular debris in the claimed method. What is excluded from the claims is a chromatography separation step prior to performing flow-injection analysis using electrospray tandem mass spectrometry. Support for this limitation can be expressly found in the Specification.

Based on the express support provided in the specification for using centrifugation and/or filtration to remove cells/cellular debris, it is respectfully submitted that it is implicit that those methods could be used to remove cells/cellular debris regardless of what the analyte is. For example, the specification states that, with respect to small molecule substrates of interest like atrazine, "cells are centrifuged and the buffer added to the supernatant. Substrate is added and cell debris is filtered off in a parallel fashion." Specification at page 33, lines 4-8. It also expressly states

> "Cells were harvested by centrifugation and resuspended into 100 µL ammonium acetate (10 mM, pH7). 6 µL of resuspended cells were transferred into a reaction well containing 100 µL of reaction buffer with atrazine (100 µM) and ammonium acetate (10 mM, pH 7). The reaction proceeded for 6 hours at room temperature under constant shaking. The reaction was quenched by adding an equal volume of methanol (100 µL). The entire reaction mixture was transferred onto a filter plate and any solid cell debris and precipitates removed by filtration. The sample were injected directly into the electrospray mass spectrometer by flow injection and analyzed by tandem mass spectrometry."

Specification at p. 39, line 28 to p. 40, line 3. Moreover, at page 33, lines 114-16, the Specification states that "[o]ligosaccharides are cleaned up by removing all ionic species using a mixed ion exchange resin. E. coli. Cells are partially lysed, and all cell debris, DNA and protein impurities are precipitated with ethanol and removed by filtration."

In his rejection under 35 U.S.C. § 102(e), the Examiner has acknowledged that the disclosure provided in priority document USSN 60/119,766 would anticipate the pending claims. See discussion in section V.C. below. The relevant disclosure from the priority document is also in the application as filed. If this disclosure would otherwise anticipate the pending claims under 35 U.S.C. § 102(e), it must also provide an adequate description of the claimed invention.

Applicants wish to further point out that claim 136 is narrower and is specifically limited to the situation where the analyte is the product of an enzymatic reaction and/or an enzyme substrate.

Applicants would like to reiterate that claim 136 is fully supported by the Specification, as filed, in view of the comments previously provided.

Accordingly, Applicants respectfully request withdrawal of the new matter rejection.

C. 35 U.S.C. § 102(e)

Claims 3, 72, 73, 77, 78, 106, 125-134, and 136-144 stand rejected under 35 U.S.C. § 102(e) as being allegedly anticipated by Stemmer et al. (U.S. Pat. No. 6,500,617B1), as evidenced by provisional application 60/119,776. This rejection is respectfully traversed.

The Examiner alleges that the Stemmer et al. '617 patent discloses all of the limitations of the pending claims. The Examiner points to the disclosure in column 53 of that patent . Applicants respectfully point out that the disclosure from col. 52, line 63 to col. 54, line 49 does not appear in the priority documents for the '617 patent. Therefore, the effective 102(e) date for that disclosure is April 22, 1999.

Moreover, the Examiner's assertion that the disclosure at column 53, second full paragraph, constitutes anticipatory disclosure supports Applicants position that their February 11, 1999 priority claim is proper. Col. 53, second full paragraph state:

> A high throughput method for detecting analyte molecules from a complex biological matrix is by electrospray tandem mass spectrometry as taught in "HIGH THROUGHPUT MASS SPECTROMETRY" by Sun ai Raillard, U.S. Pat. No. [sic] 60/119,766, filed Feb. 11, 1999. In the '766 application, methods which utilize off-line parallel sample purification and fast flow-injection analysis, typically reducing the time of analysis to 30 to 40 seconds per sample.

Col. 53, second full paragraph.

In his rejection, the Examiner states that

> Stemmer et al. disclose separating the cells or cell debris thereof from one or more component of interest using centrifugation or filtration in parallel fashion to provide samples (e.g., **see column 53, second full paragraph disclosing the filtration/centrifugation method set forth in the '766 Raillard application; see also '766 application, pages 21-23, section VI; especially page 22, paragraphs 1-3; disclosing filtration and/or centrifugation techniques**). Stemmer et al. also disclose performing flow injection analysis using electrospray tandem mass spectrometry on the samples from step iii to obtain mass to charge ratio data for the component of interest wherein the component of interest (**e.g., see column 53, second full paragraph**). In addition, Stemmer et al. also disclose a component

> use of a component of interest selected from the group consisting of an inorganic ion, secondary metabolite, protein binding molecule, carbohydrate, carbohydrate binding molecule, an enzyme, an enzyme substrate product of an enzyme catalyzed reaction, nucleic acid and product of nucleic acid catalyzed reaction (e.g., see Example 7 wherein a protease inhibitor i.e., a protein binding molecule is disclosed; see also abstract and examples wherein "protein binding" toxin molecules are disclosed). Finally, Stemmer et al. disclose methods wherein the component of interest has not undergone chromatographic separation prior to step iv (e.g., see Example 10; see also column 53, second full paragraph; **see also '766 application, section VI as noted above; see also summary of invention**).

Office Action at p. 9, line 6 to p. 10, line 2 (emphasis added).

In view of the fact that Applicants have a priority claim to USSN 60/119,776 and all of the relevant disclosure from the Stemmer '617 patent is derived from its reference to USSN 60/119,776, the Stemmer '617 patent cannot anticipate the pending claims. Accordingly, withdrawal of this rejection is respectfully requested.

D. 35 U.S.C. § 103

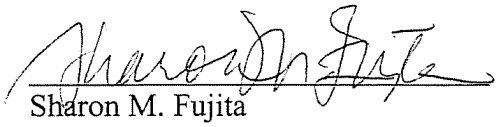
Claims 3-6, 23-26, 72, 73, 77, 78, 106-109, 115-116 and 125-144 stand rejected under 35 U.S.C. § 103(a) for being allegedly unpatentable over the Stemmer '617 patent, in view of Favretto et al. This rejection is respectfully traversed.

As explained in part C above, the description relied on in the Stemmer '617 patent is not prior art to the subject claims. The Favretto et al. reference, which is being cited for its alleged disclosure on neutral loss mass spectrometry and simultaneous quantitation of the product of an enzyme reaction and enzyme substrate does not render the claimed invention obvious. Accordingly, withdrawal of this rejection is respectfully requested.

CONCLUSION

In light of the foregoing submissions, favorable action on all claims is earnestly solicited. Should the Examiner believe that a telephone conference would expedite the prosecution of this application, the undersigned can be reached at the telephone number set forth below. The Commissioner is hereby authorized to charge any deficiency in fees or credit any overpayment to Deposit Account No. 50-0990.

October 18, 2007

By: 
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